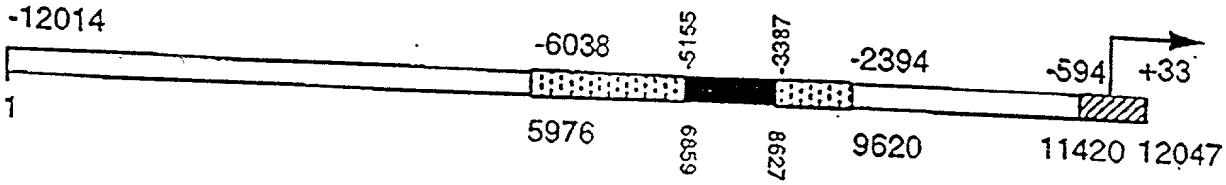

-12014
-6038
-5155
-3387
-2394
-594
+33
1
5976
6859
8627
9620
11420
12047

FIGURE 1

```
HKLK2.LA0      ( 6998)  AA-CTGAGCCTTGATTATATTG-GAGCTTGGTTGCA-CAG-ACATGTCGA
                        :: :: :: : ::: :::: :: : :::       :  ::: :::  :: :
PSE            (  509)  AATCT-AG-C-TGA-TATAGTGTG-GCTCAAAACCTTCAGCACAAATC-A

HKLK2.LA0      ( 7044)  CCACCTTCATGGCTGAACTTTAGTACTTAGCCCCTCCAGACGTCTACAGC
                         :::: : : : ::  : : : ::   : :   : ::: ::  :: :::
PSE            (  553)  -CACCGTTA-GACT--A-TCTGGT--GT-G--GC-CCAAAC--CTTCAGG

HKLK2.LA0      ( 7094)  TGATAGGCTGTAACCCAACAT-TGTCACCATAAATCACATTGTTAGACTA
                        ::: :    :  :: : : :: :: ::  :: : :: ::     :: : :
PSE            (  590)  TGA-ACAAAGGGACTCTA-ATCTGGCAGGAT-ATTC-CA----AAG-C-A

HKLK2.LA0      ( 7143)  TCCAGTG-TGGCC-CAAGCTCCCGTGTAAACACAGGCACTCTAAACAG--
                        :  :: : :: :: : ::   :   ::: : : : :    ::: ::
PSE            (  630)  T-TAGAGATGACCTCTTGC-AAAG-AAAAAGAAATGGAAAAGAAAAAGAA

HKLK2.LA0      ( 7189)  -G-CAGGATATTTCAAAAGCTT-AGAGATGACCTCCCAGGAGCTGAATGC
                         :  :::: :    ::::     :::::::::::: ::::  ::::  :
PSE            (  677)  AGAAAGGAAAAAAAAAAAAAAAAAGAGATGACCTCTCAGGCTCTGAGGGG

HKLK2.LA0      ( 7236)  AAA-GACCTGGCCTCTTTGGGCAAGGAGAATCCTTTACCGCACACTCTCC
                        ::: : ::::   :::::: :::::: : :::: :   ::::: :::::
PSE            (  727)  AAACG-CCTGAGGTCTTTGAGCAAGGTCAGTCCTCTGTTGCACAGTCTCC

HKLK2.LA0      ( 7285)  TTCACAGGGTTATTGTGAGGATCAAATGTGGTCATGTGTGTGAGACACCA
                         ::::::::: ::::::: ::::::::::::::: :::: :::: :::::
PSE            (  776)  CTCACAGGGTCATTGTGACGATCAAATGTGGTCACGTGTATGAGGCACCA
                                  :  --                 :::      -

HKLK2.LA0      ( 7335)  GCACATGTCTGGCTGTGGAGAGTGACTTCTA--TGTGTGCTAACATTGCT
                        ::::::: :::::: ::: ::::: : : ::  ::: ::::  :: ::::
PSE            (  826)  GCACATGCCTGGCTCTGGGGAGTGCCGTGTAAGTGTATGCTTGCACTGCT
                        :: : :    :    ::  :     :::  : : : :          :

HKLK2.LA0      ( 7383)  GAGTGCTAAGAAAGTATTAGGCATGGCT-TTCAGCACTCACAGATGCTCA
                        :: ::::  : : :: : ::: ::   : ::::::::: ::::::::::
PSE            (  876)  GAATGCTTGGGATGTGTCAGGGAT-TATCTTCAGCACTTACAGATGCTCA
                           ::    :          :      :     :   ::
```

FIGURE 2A

```
HKLK2.LA0    ( 7432)  TCTAATCCTCACAACATGGCTACAGGG-TGGGCACTACTAGCCTCATTTG
                      ::: :::::::::: :::  :::  ::: :::: : :::: ::::::::::
PSE          (  925)  TCTCATCCTCACAGCATCACTA-TGGGATGGGTATTACTGGCCTCATTTG
                      :  ::     : ::  :        :::     :  : :::     : :

HKLK2.LA0    ( 7481)  ACAGAGGAAAG-GACTGTGGATAAGAAGGGGGGTGACCAATAGGTCAGAGT
                      :  :: ::::: : :::::: : :::: :::: ::::: :::   ::: :
PSE          (  974)  ATGGA-GAAAGTGGCTGTGGCTCAGAAAGGGGGGACCACTAGACCAGGGA
                           :  : : :        :   :         :    :

HKLK2.LA0    ( 7530)  CATTCTGGATGCAAGGGG-CTCCAGAGGACCATGATTAGACATTGTCTGC
                      :: :::::::::  :::: :::::::: ::::::::  :  ::    ::::
PSE          ( 1023)  CACTCTGGATGC-TGGGGACTCCAGA-GACCATGACCACTCACCAACTGC
                        :  :           :    :    ::   ::      :

HKLK2.LA0    ( 7579)  AGAGAAATT----ATGG-CTGGATGTCTCTGCCCCGGAAAGGG-GGA--T
                      :::::::::     ::: :: :::::: ::: :: ::: :::: ::: :
PSE          ( 1071)  AGAGAAATTAATTGTGGCCT-GATGTCCCTGTCCTGGAGAGGGTGGAGGT
                        :: :     :   :  :: :      :  :     ::    ::

HKLK2.LA0    ( 7621)  GCACTTTCCTTGACCCCCTATCTCAGATCTTGACTTTGAG-GTTATCTCA
                      : :: :::  : ::: :::: ::  :: : :  :::: :: : : : :: _
PSE          ( 1120)  GGACCTTCACTAACCTCCTACCT-TGACCCTCTCTTTTAGGGCTCTTTCT
                      :  :    :  :  :        :: :      : :             :

HKLK2.LA0    ( 7670)  GACTTCCTCTATGATACCAGGAGCCCATCATAATCTCTCTGTGTCCTCTC
                      ::: ::: : ::: ::: :::: :::  :::  : : :::::  :: ::
PSE          ( 1169)  GACCTCCACCATGGTACTAGGA-CCC--CATTGTAT-TCTGT-ACC-CT-
                      ::     :  :                ::  ::    : :  : :

HKLK2.LA0    ( 7720)  CCCTTCCTCAGTCTTACTG-CCCACTCTTCCCAGCTCCATCTCCAGCTGG
                       : :  : : :: :: :: ::: : :: :::: :: ::  :::::::
PSE          ( 1212)  --C-T--TGACTC-TA-TGACCCCCACTGCCCA-CTGCA--TCCAGCT--
                         :    :       :  :    :         ::        :

HKLK2.LA0    ( 7769)  CCAGGTGTAGCCACAGTACCTAACTCT-TTGCAGAGAACTATAAATGTGT
                        :: ::  :: :  : :::: :::: :: :  ::  ::    : :::
PSE          ( 1250)  ---GG-GT--CC-C-CT-CCTATCTCTATT-CCCAG--CTGGCCA-GTGC
                        :          :       ::  _             :

HKLK2.LA0    ( 7818)  A-TCCTACAGGGGAGAAAAAAA-AAAAG-AACTCTGAAAGAGCTGACATT
                      : : :: ::: :  :          :: ::::::::: : :::::::::
PSE          ( 1287)  AGT-CT-CAGTGCCCACCT~~GT~~TTGTCAGTAACTCTGAAGGGGCTGACATT
                        :  :       :   ::  ::     :                 :

HKLK2.LA0    ( 7865)  TTACCGACTTGCAAACACATAAGCTAACCTGCCAG--TTTTGT----GCT
                      :::: :::::::::::: :::::::::: : ::::  ::::::     :::
PSE          ( 1335)  TTACTGACTTGCAAACAAATAAGCTAACTTTCCAGAGTTTTGTGAATGCT
                      :  :  :  :: :  :          ::        : :   :  : : :

HKLK2.LA0    ( 7909)  GGTAGAACT-CATGAGACTCCTGGGTCAGAGGCAAAAGATTTTATTACCC
                      :: :: : : :::::::::::: :::::::::::: : ::::: : : :
PSE          ( 1385)  GGCAG-AGTCCATGAGACTCCTGAGTCAGAGGCAAAGGCTTTTACTGCTC
                      :            :::      :::   ::
```

Docket No. 5050-0-PCT

FIGURE 2B

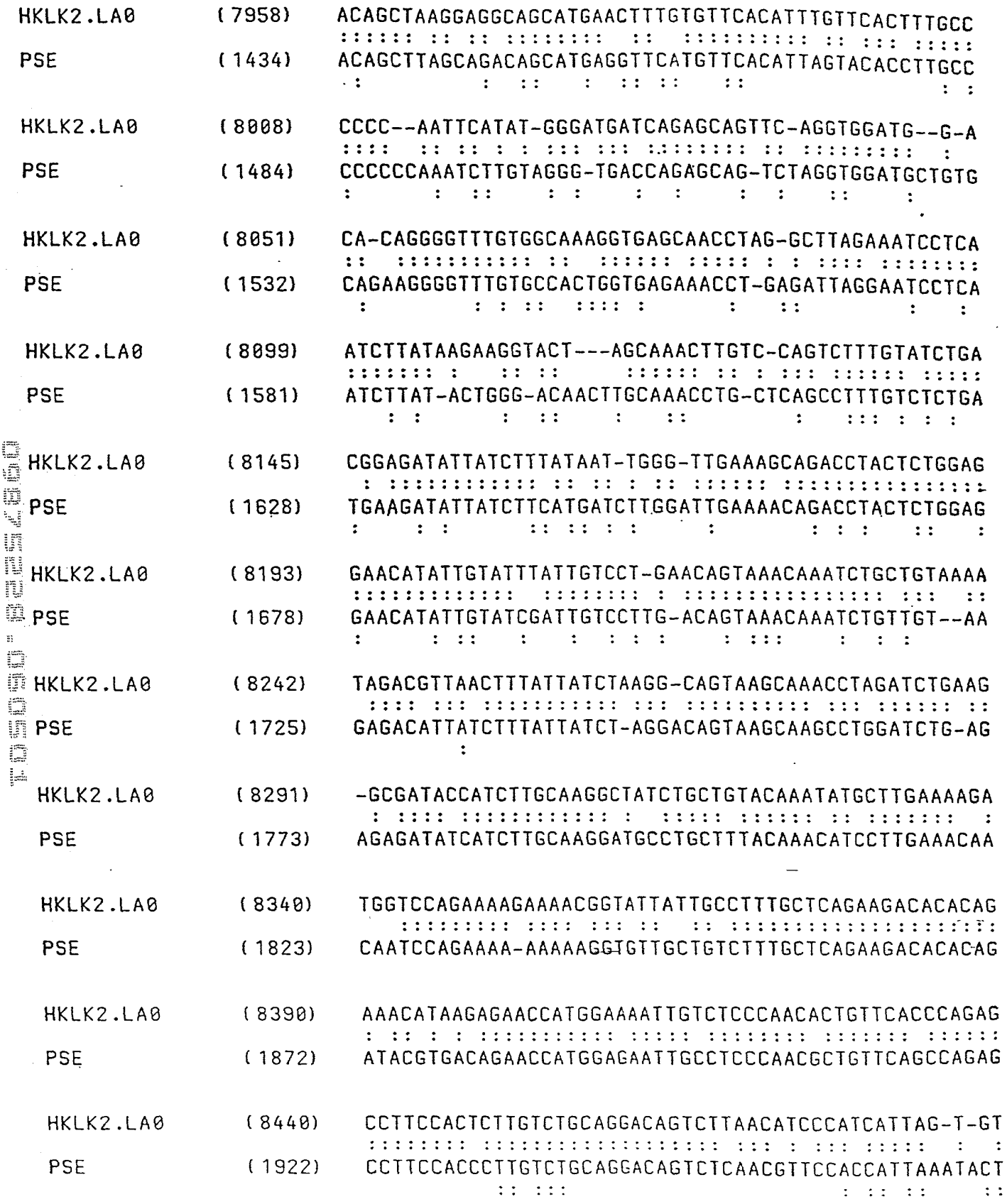

HKLK2.LA0 (7958) ACAGCTAAGGAGGCAGCATGAACTTTGTGTTCACATTTGTTCACTTTGCC
PSE (1434) ACAGCTTAGCAGACAGCATGAGGTTCATGTTCACATTAGTACACCTTGCC
HKLK2.LA0 (8008) CCCC--AATTCATAT-GGGATGATCAGAGCAGTTC-AGGTGGATG--G-A
PSE (1484) CCCCCCAAATCTTGTAGGG-TGACCAGAGCAG-TCTAGGTGGATGCTGTG
HKLK2.LA0 (8051) CA-CAGGGGTTTGTGGCAAAGGTGAGCAACCTAG-GCTTAGAAATCCTCA
PSE (1532) CAGAAGGGGTTTGTGCCACTGGTGAGAAACCT-GAGATTAGGAATCCTCA
HKLK2.LA0 (8099) ATCTTATAAGAAGGTACT---AGCAAACTTGTC-CAGTCTTTGTATCTGA
PSE (1581) ATCTTAT-ACTGGG-ACAACTTGCAAACCTG-CTCAGCCTTTGTCTCTGA
HKLK2.LA0 (8145) CGGAGATATTATCTTTATAAT-TGGG-TTGAAAGCAGACCTACTCTGGAG
PSE (1628) TGAAGATATTATCTTCATGATCTTGGATTGAAAACAGACCTACTCTGGAG
HKLK2.LA0 (8193) GAACATATTGTATTTATTGTCCT-GAACAGTAAACAAATCTGCTGTAAAA
PSE (1678) GAACATATTGTATCGATTGTCCTTG-ACAGTAAACAAATCTGTTGT--AA
HKLK2.LA0 (8242) TAGACGTTAACTTTATTATCTAAGG-CAGTAAGCAAACCTAGATCTGAAG
PSE (1725) GAGACATTATCTTTATTATCT-AGGACAGTAAGCAAGCCTGGATCTG-AG
HKLK2.LA0 (8291) -GCGATACCATCTTGCAAGGCTATCTGCTGTACAAATATGCTTGAAAAGA
PSE (1773) AGAGATATCATCTTGCAAGGATGCCTGCTTTACAAACATCCTTGAAACAA
HKLK2.LA0 (8340) TGGTCCAGAAAAGAAAACGGTATTATTGCCTTTGCTCAGAAGACACACAG
PSE (1823) CAATCCAGAAAA-AAAAAGGTGTTGCTGTCTTTGCTCAGAAGACACACAG
HKLK2.LA0 (8390) AAACATAAGAGAACCATGGAAAATTGTCTCCCAACACTGTTCACCCAGAG
PSE (1872) ATACGTGACAGAACCATGGAGAATTGCCTCCCAACGCTGTTCAGCCAGAG
HKLK2.LA0 (8440) CCTTCCACTCTTGTCTGCAGGACAGTCTTAACATCCCATCATTAG-T-GT
PSE (1922) CCTTCCACCCTTGTCTGCAGGACAGTCTCAACGTTCCACCATTAAATACT

FIGURE 2C

```
HKLK2.LA0      ( 8488)  --GTCTACCACATCTGGCTTCACCGTGCCTAACCAAGATTTCTAGGTCCA
                        ;:::: :::::: :::::    :::::::::::: ::::::::::
PSE            ( 1972)  TCTTCTATCACATCCTGCTTCTTTATGCCTAACCAAG-GTTCTAGGTCCC
                              :       ::    : :   :      : :   :: :::   :

HKLK2.LA0      ( 8536)  GTTCCCCACCATGTTTGGCAGTGCCCCACTGCCAACCCCAGAATAAGGGA
                        : :   : ::  ::: :::::::  : :::::::::: :::::::::::: :
PSE            ( 2021)  GAT--CGACTG1GTCTGGCAGCACTCCACTGCCAAACCCAGAATAAGGCA
                              ::   :   :: :   :      ::                :   :

HKLK2.LA0      ( 8586)  GTGCTCAGAATTCCGA
                        : :::::: :: ::::
PSE            ( 2069)  GCGCTCAGGATCCCGA
                        :             : :
```

09975268 - 050604

FIGURE 2D

T0S090'8225/8660

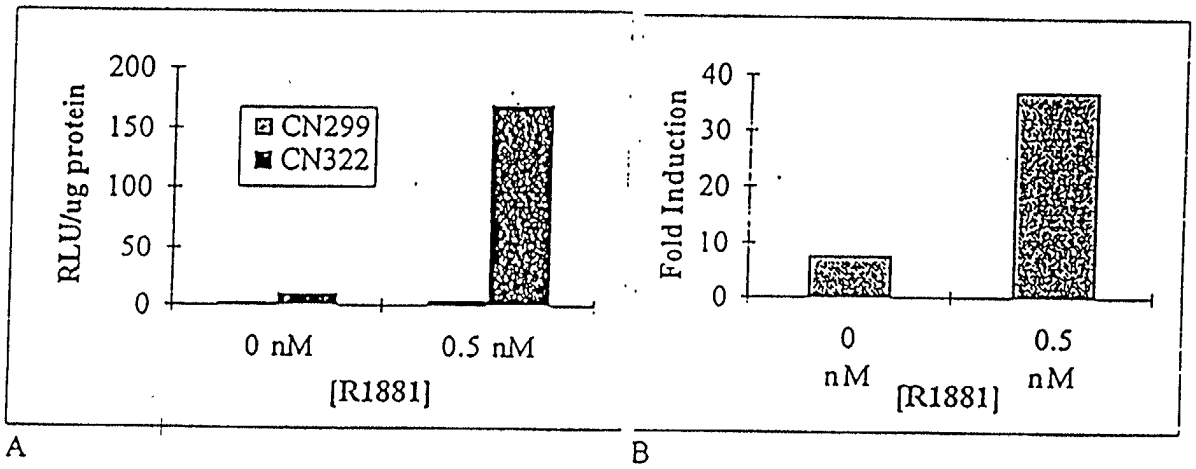


FIGURE 3

TOSO90 "0221260

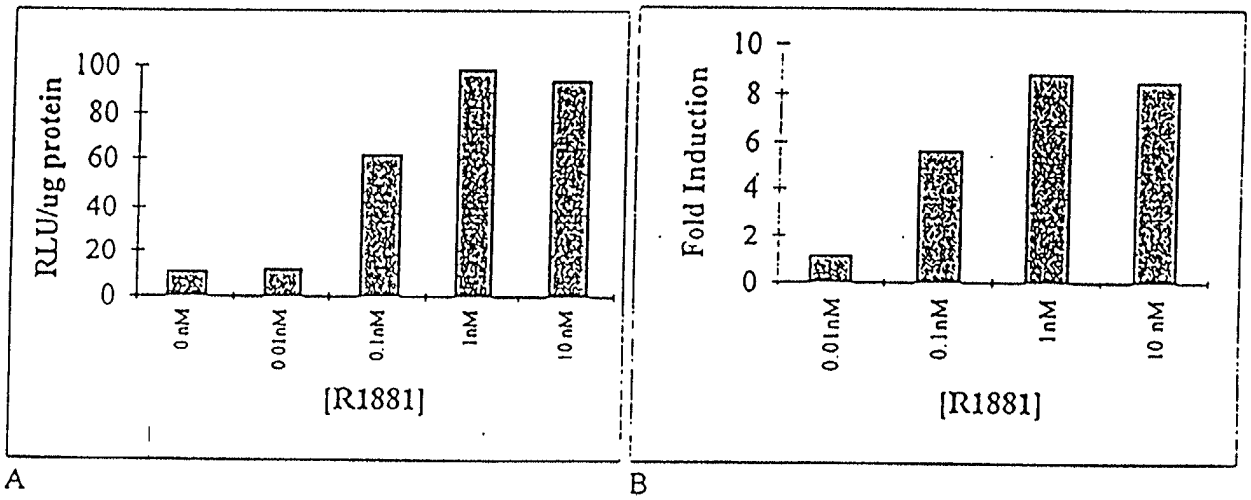


FIGURE 4

EP0509035A2

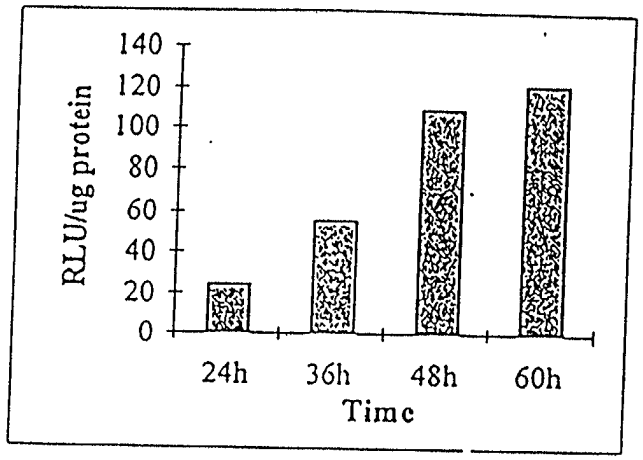


FIGURE 5

TOSO90 .3625280

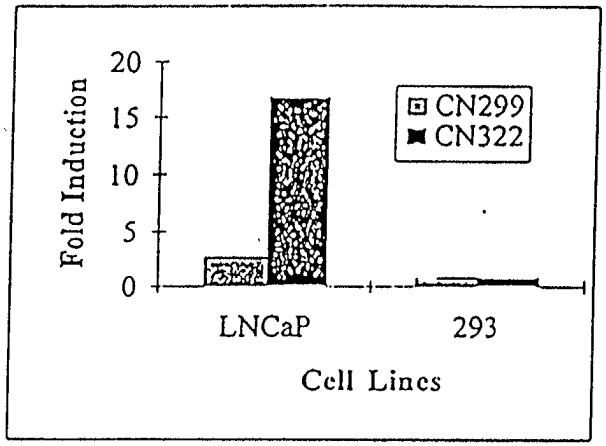


FIGURE 6

T0S090 "B22972860

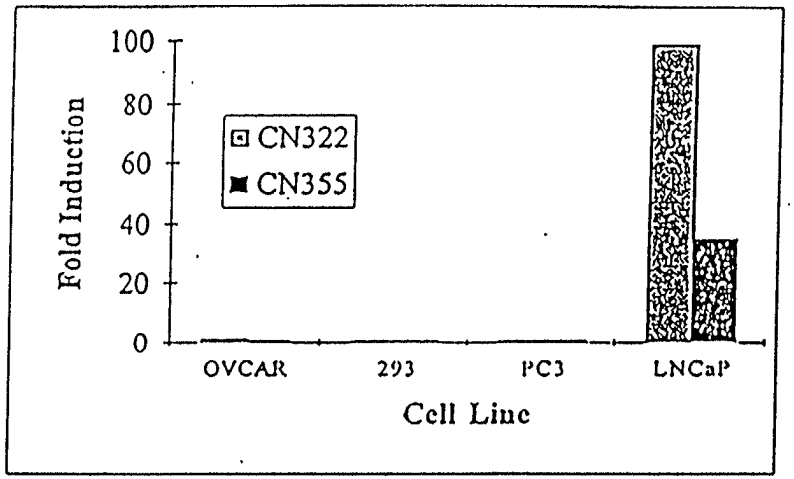


FIGURE 7

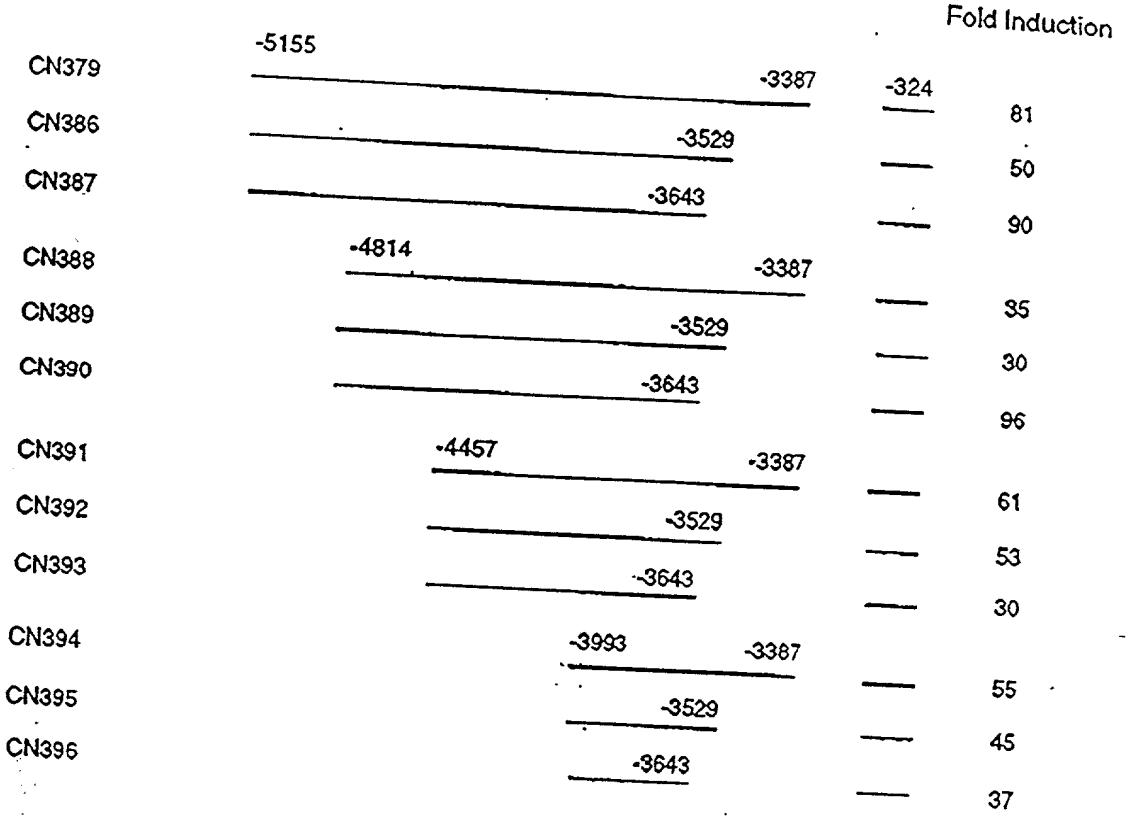

Fold Induction
-5155
CN379
-3387
-324
81
CN386
-3529
50
CN387
-3643
90
-4814
CN388
-3387
35
CN389
-3529
30
CN390
-3643
96
-4457
CN391
-3387
61
CN392
-3529
53
CN393
-3643
30
CN394
-3993
-3387
55
CN395
-3529
45
CN396
-3643
37

FIGURE 8

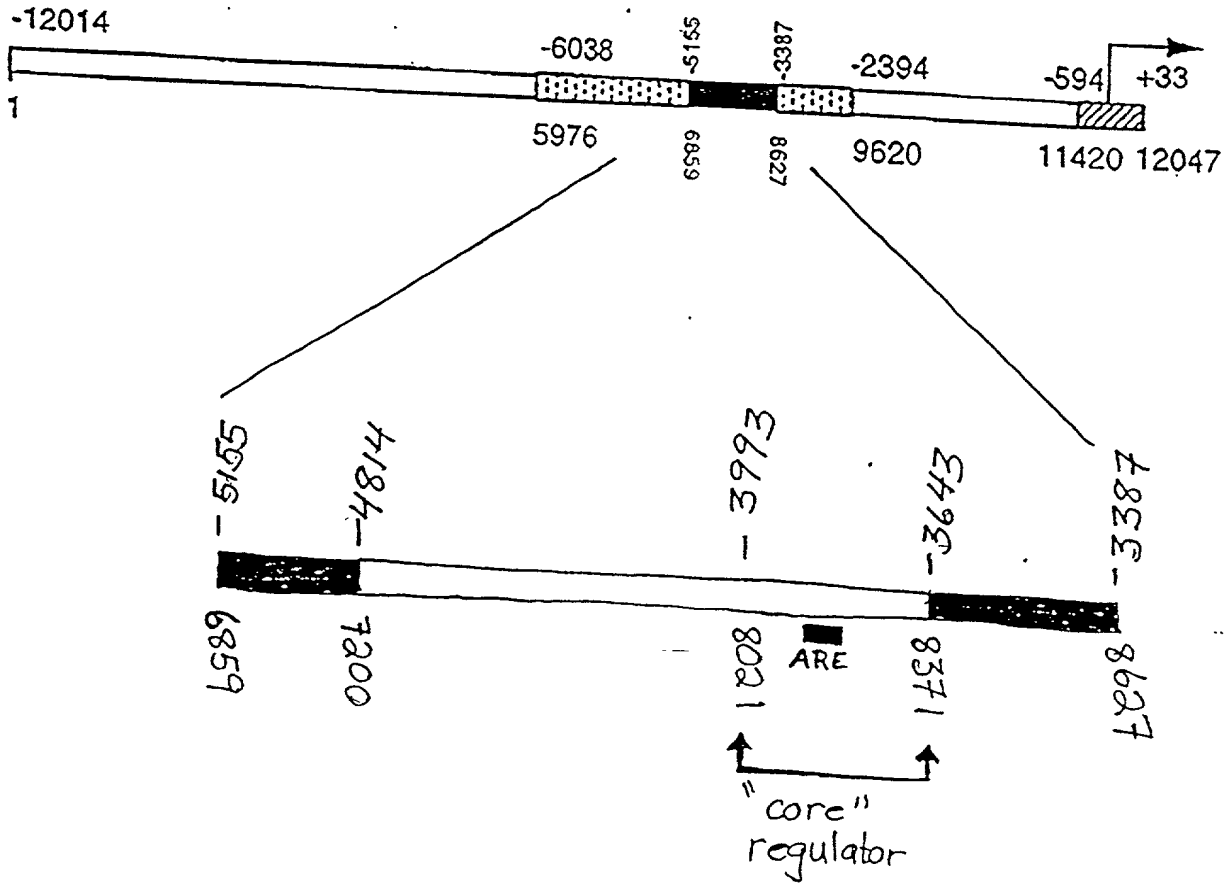
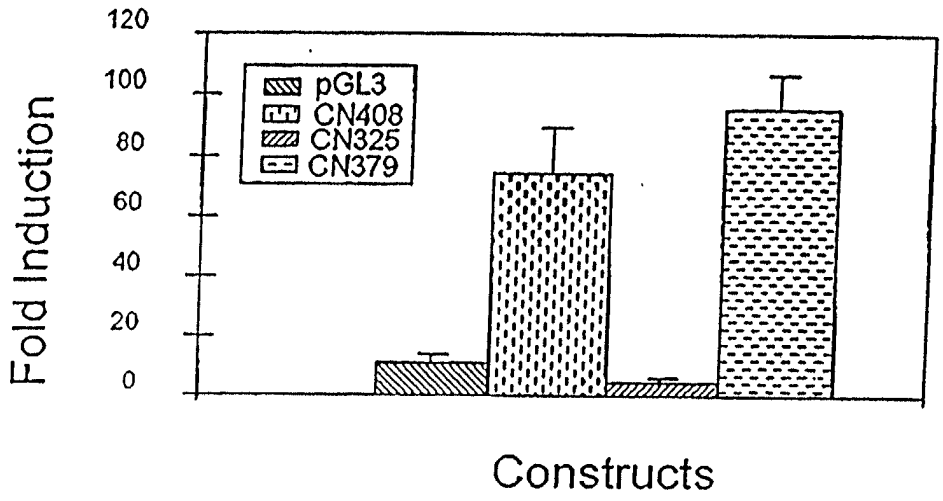

-12014
1
-6038
-5155
-3387
-2394
-594
+33
5976
6859
8627
9620
11420 12047
-5155
-4814
-3993
-3643
-3387
6859
7200
8021
ARE
8371
8627
"core"
regulator

FIGURE 9

TOSO90 82252860

A



B

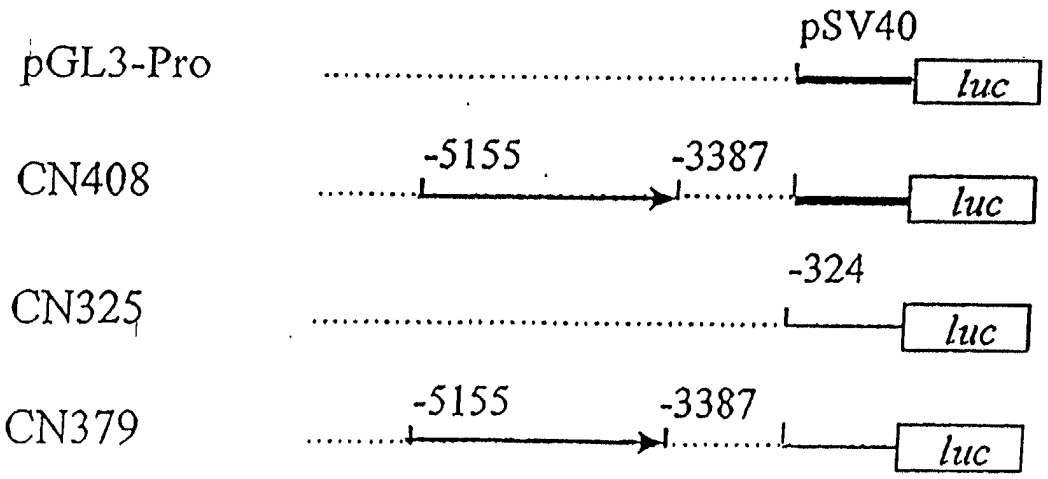


FIGURE 10

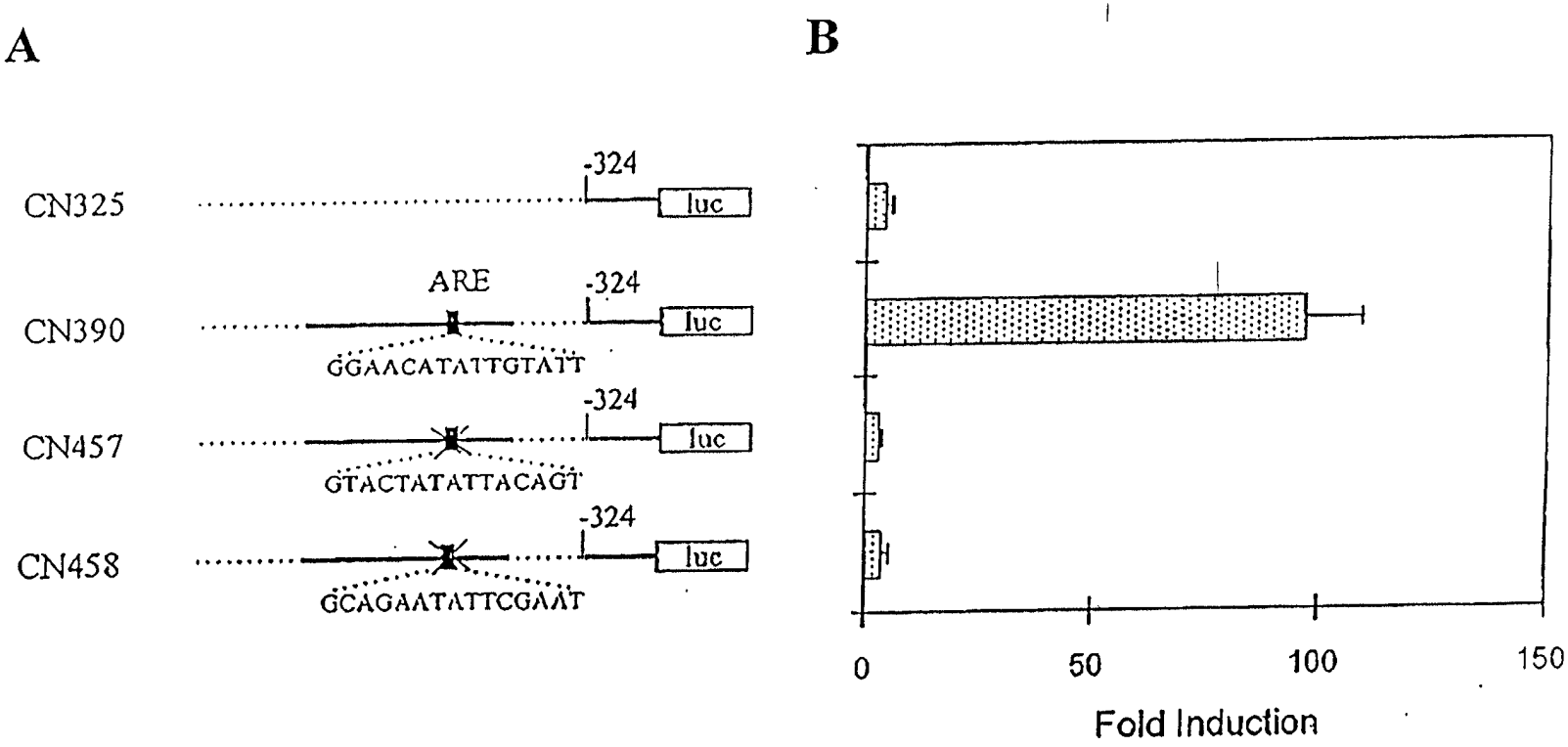

A
CN325
-324
luc
ARE
CN390
-324
luc
GGAACATATTGTATT
CN457
-324
luc
GTACTATATTACAGT
CN458
-324
luc
GCAGAATATTCGAAT
B
0
50
100
150
Fold Induction

FIGURE 11

T0S090" 8225Z860

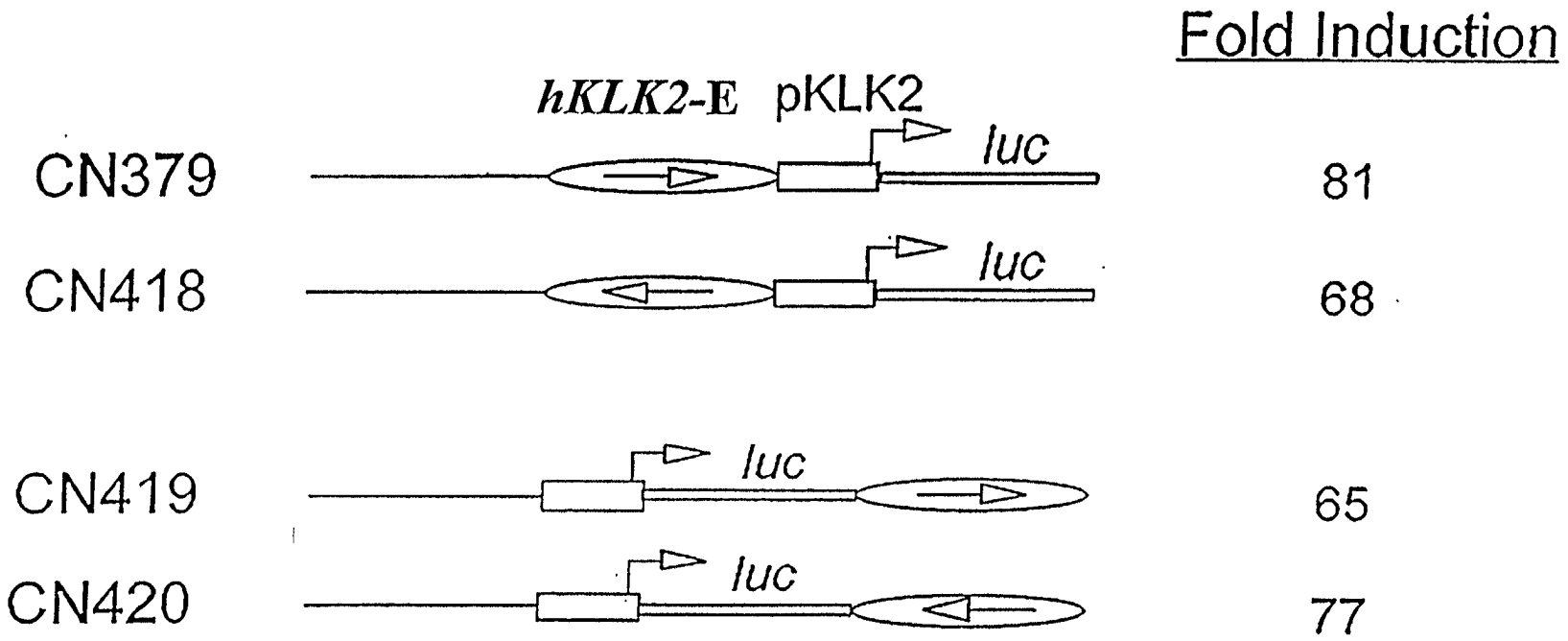


FIGURE 12

TOSO90 B225860

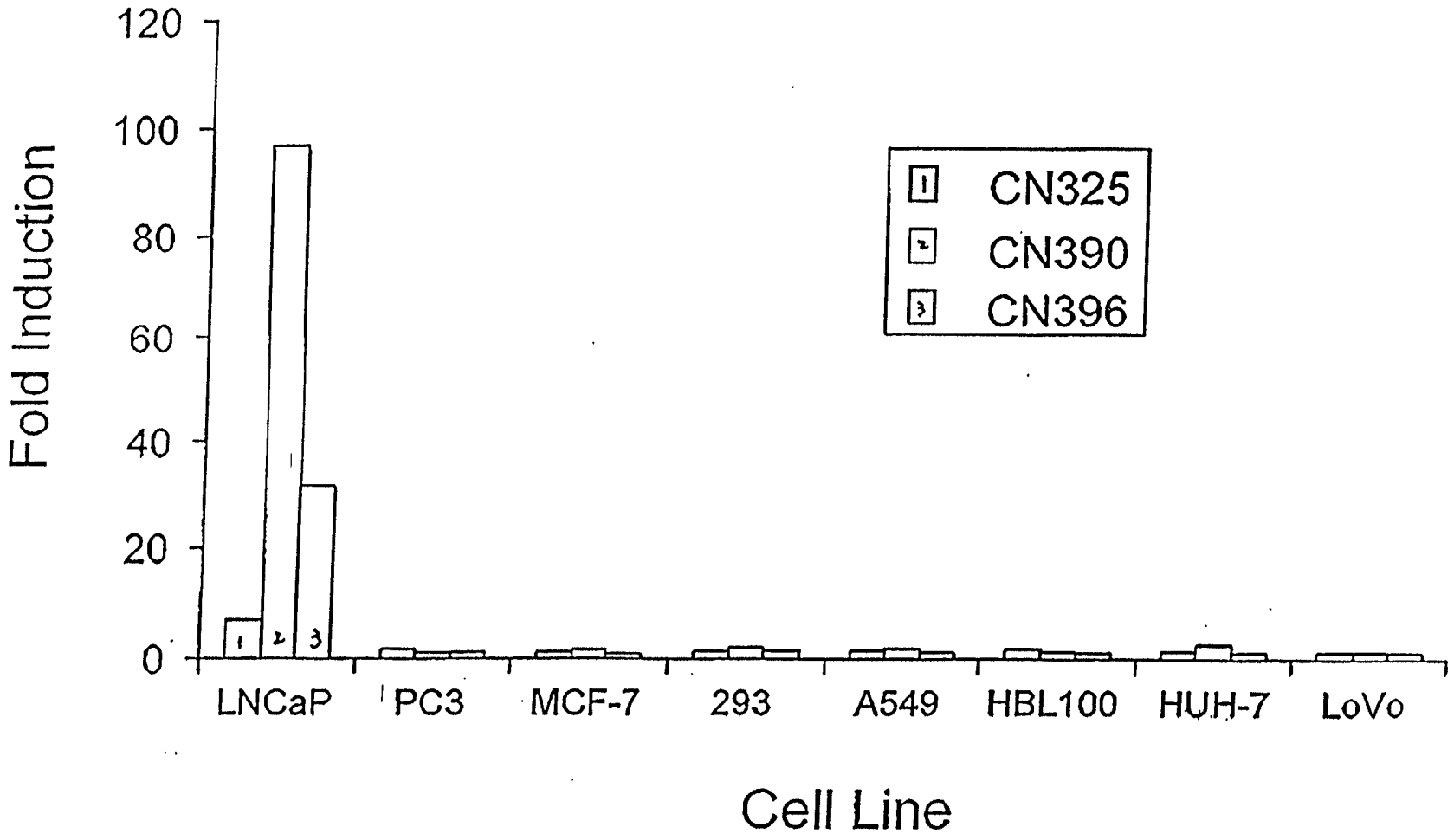


FIGURE 13

TOSD90 B225860

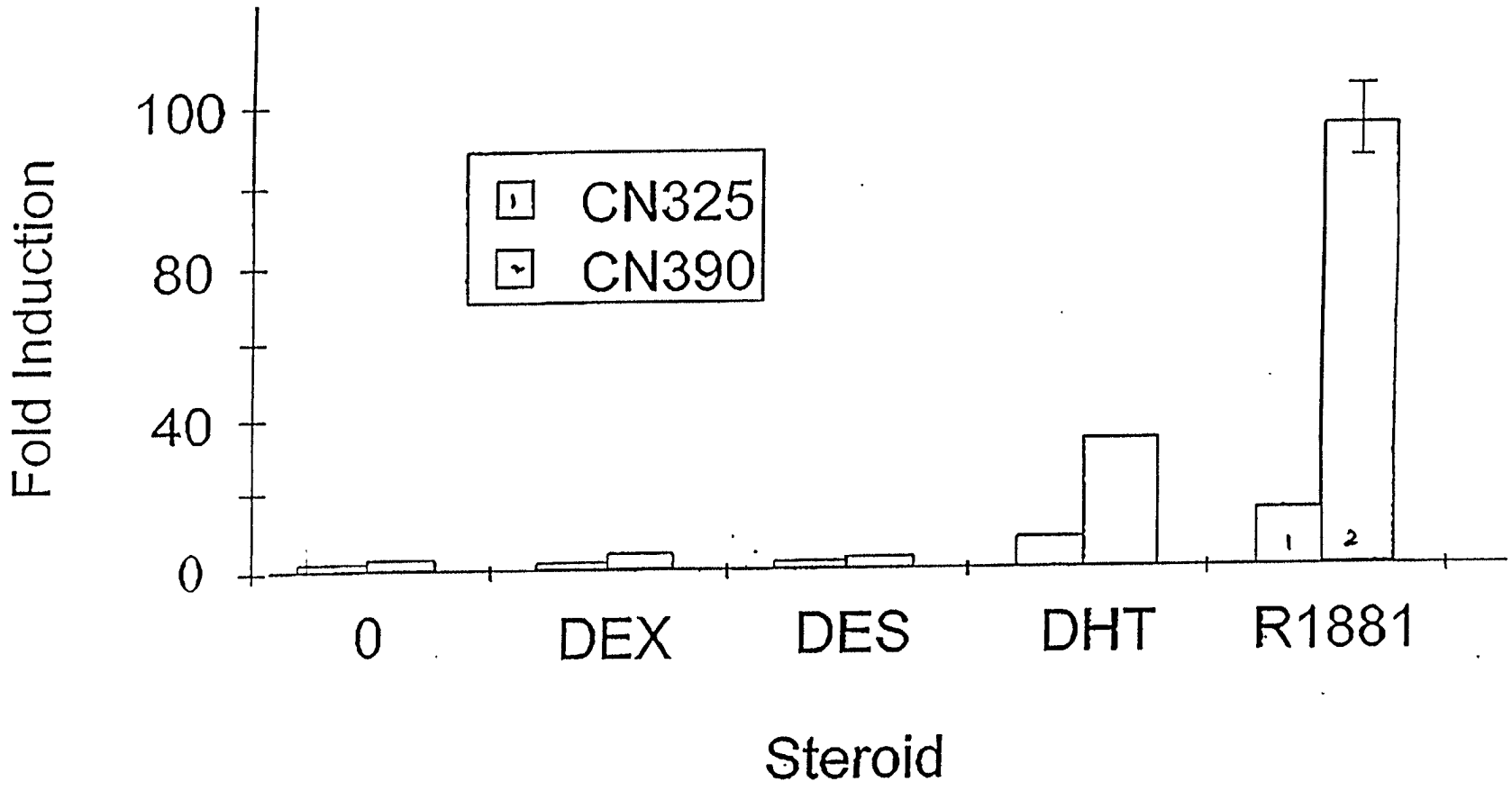


FIGURE 14

T0S090 8825860

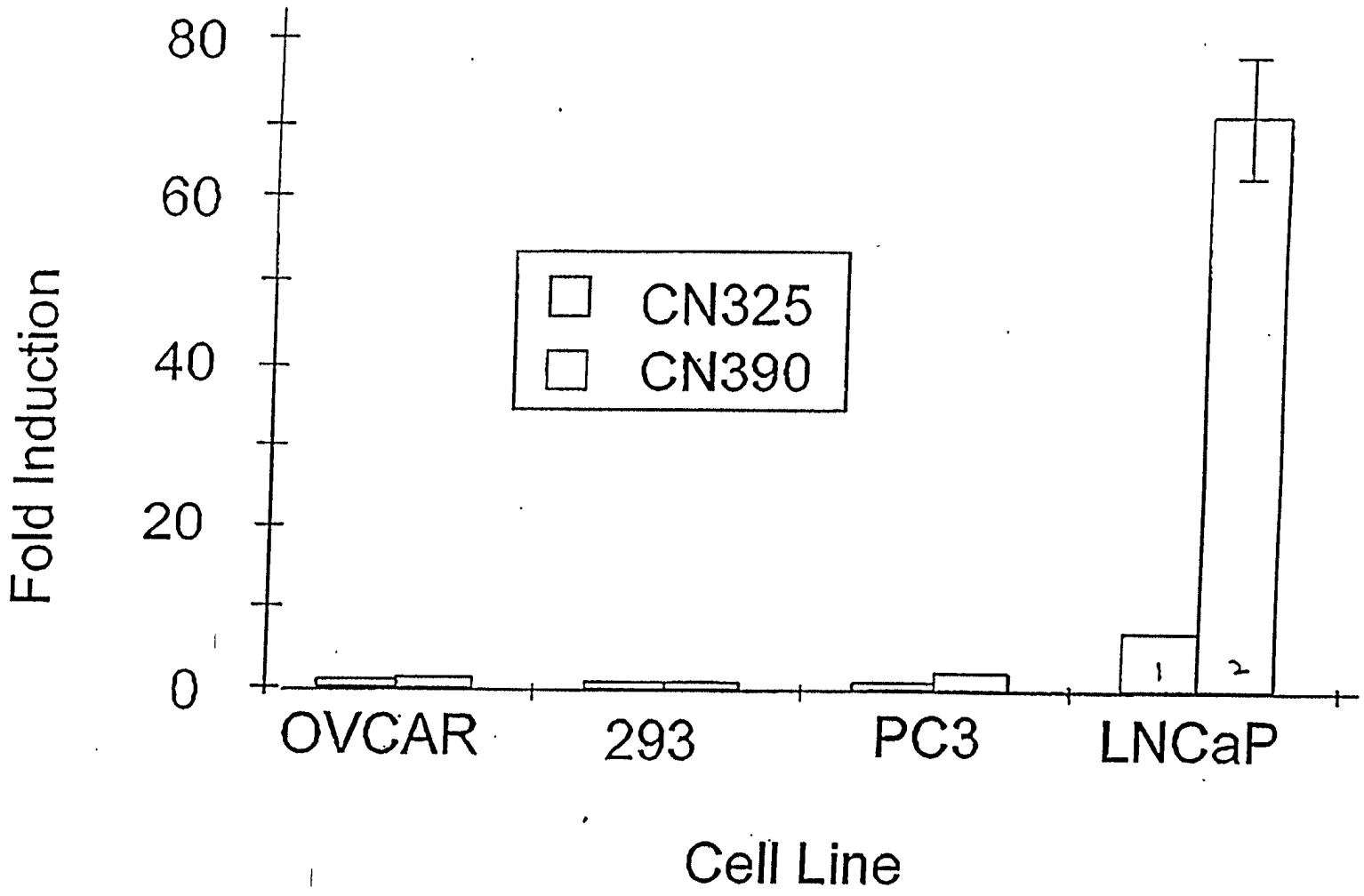


FIGURE 15

T05090 "82257860

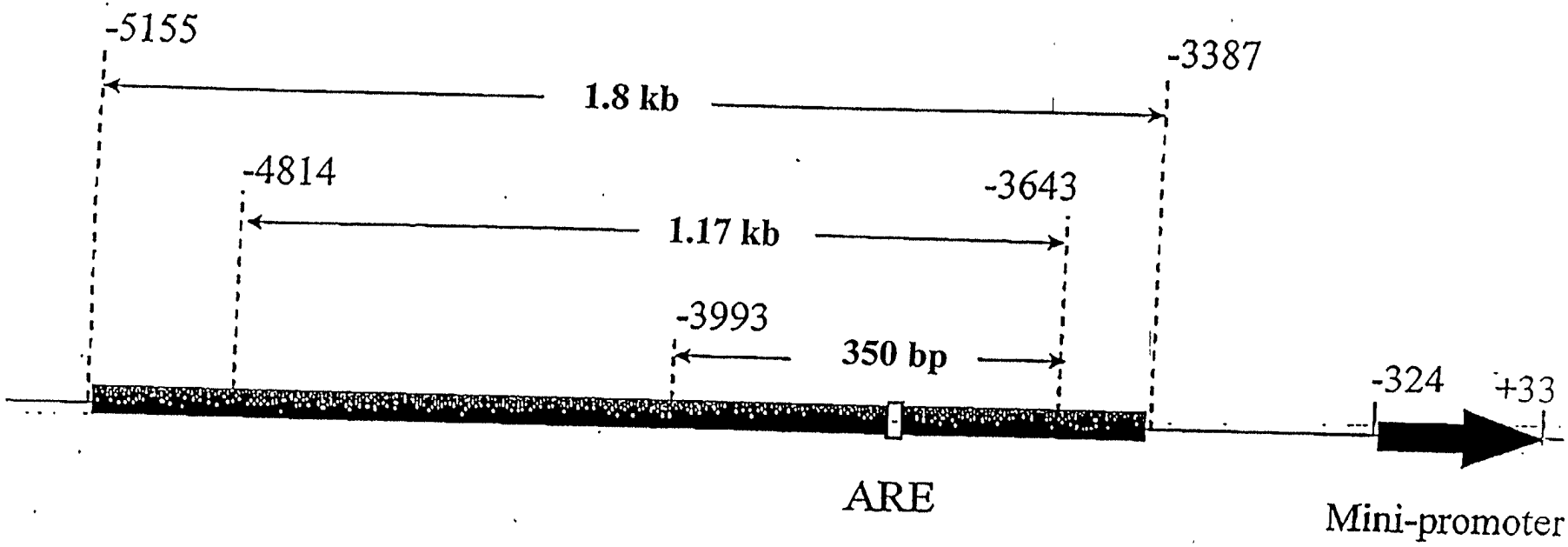


FIGURE 16

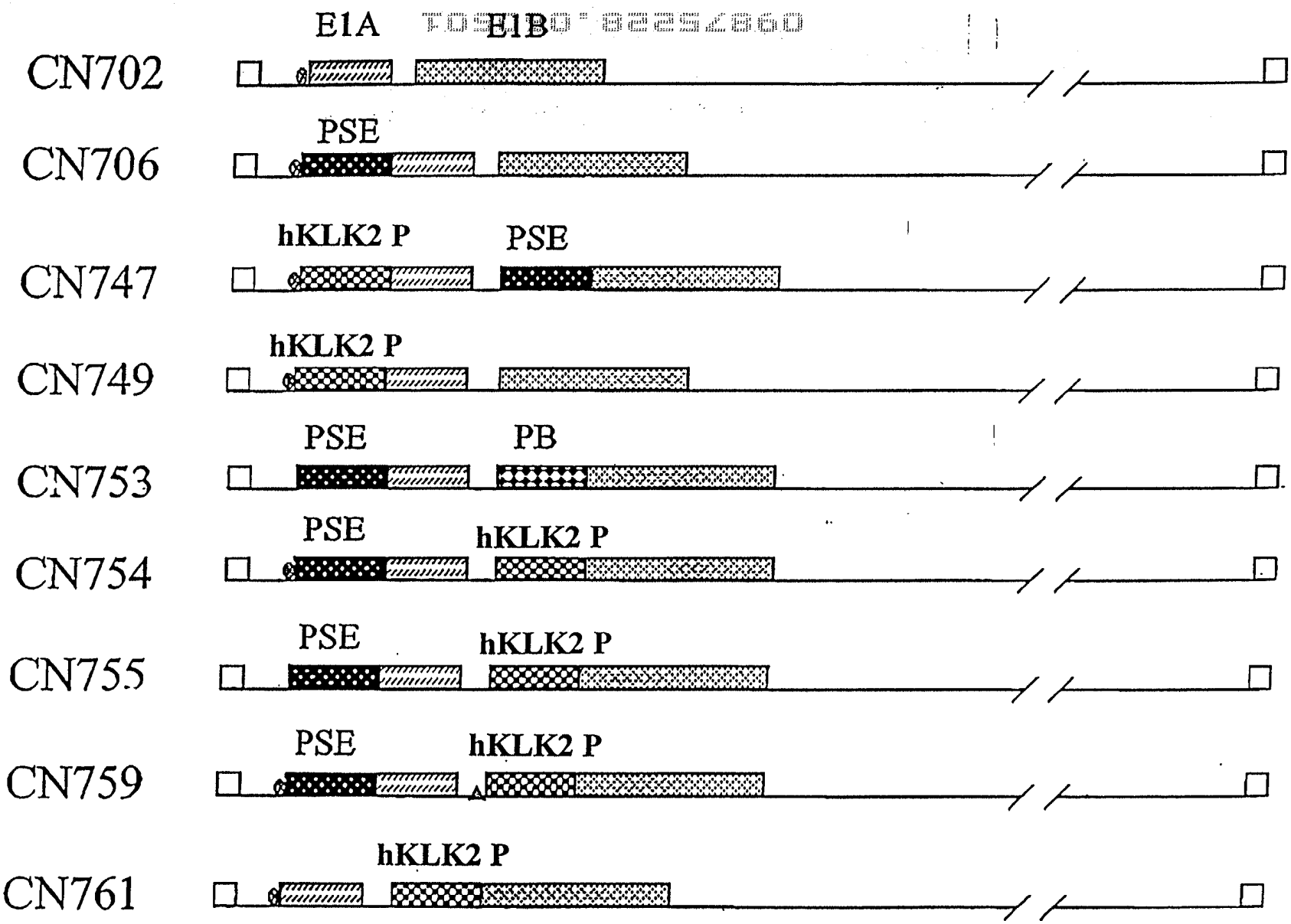

E1A
E1B
CN702
PSE
CN706
hKLK2 P
PSE
CN747
hKLK2 P
CN749
PSE
PB
CN753
PSE
hKLK2 P
CN754
PSE
hKLK2 P
CN755
PSE
hKLK2 P
CN759
hKLK2 P
CN761

FIGURE 17A

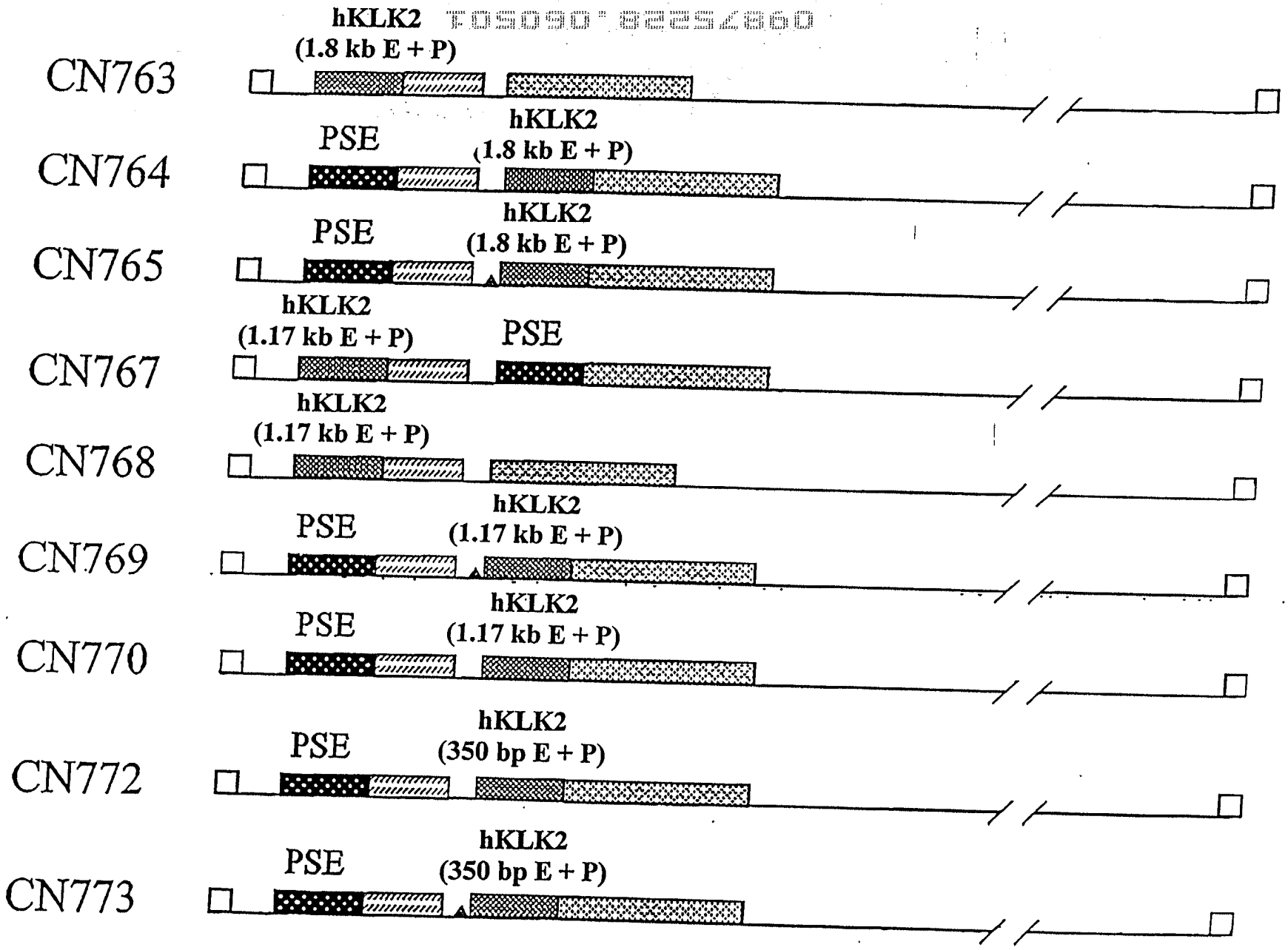

hKLK2
(1.8 kb E + P)
CN763
PSE
hKLK2
(1.8 kb E + P)
CN764
PSE
hKLK2
(1.8 kb E + P)
CN765
hKLK2
(1.17 kb E + P)
PSE
CN767
hKLK2
(1.17 kb E + P)
CN768
PSE
hKLK2
(1.17 kb E + P)
CN769
PSE
hKLK2
(1.17 kb E + P)
CN770
PSE
hKLK2
(350 bp E + P)
CN772
PSE
hKLK2
(350 bp E + P)
CN773

FIGURE 17B

EP 0 850 90 A2 2 5 7 8 6 0

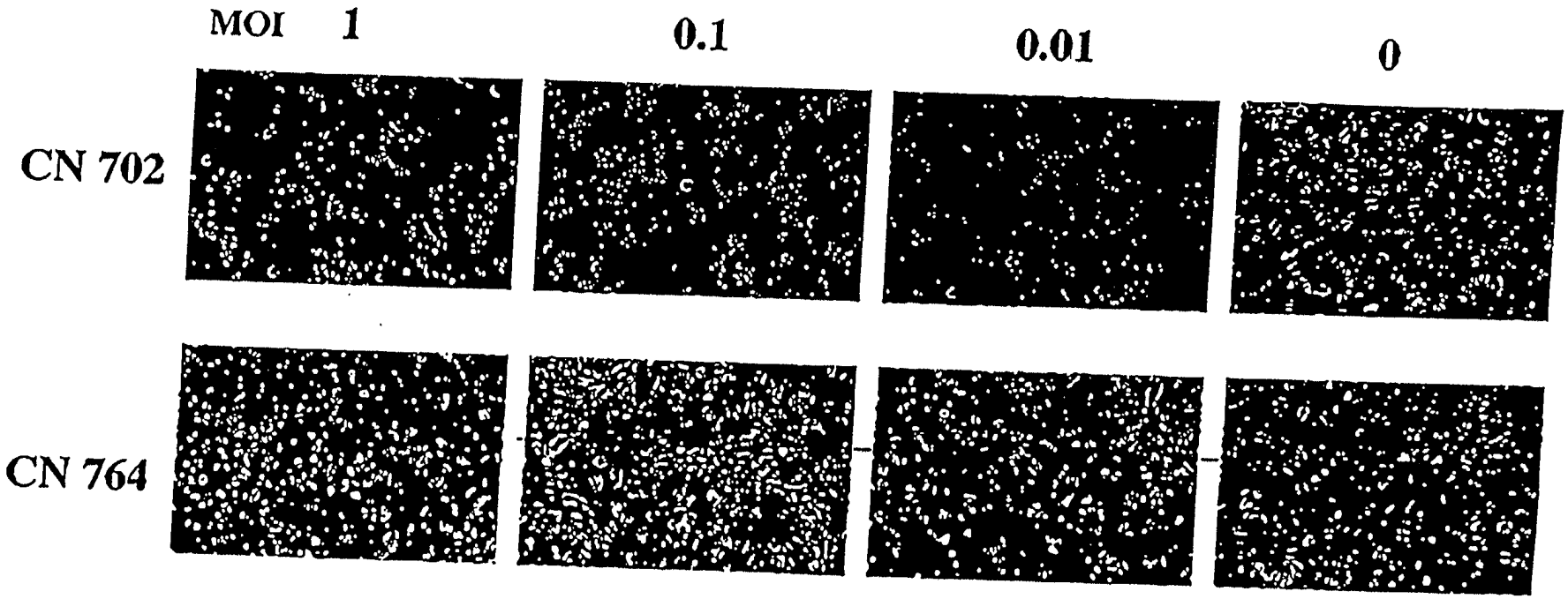


FIGURE 18

TOS090 "32251860

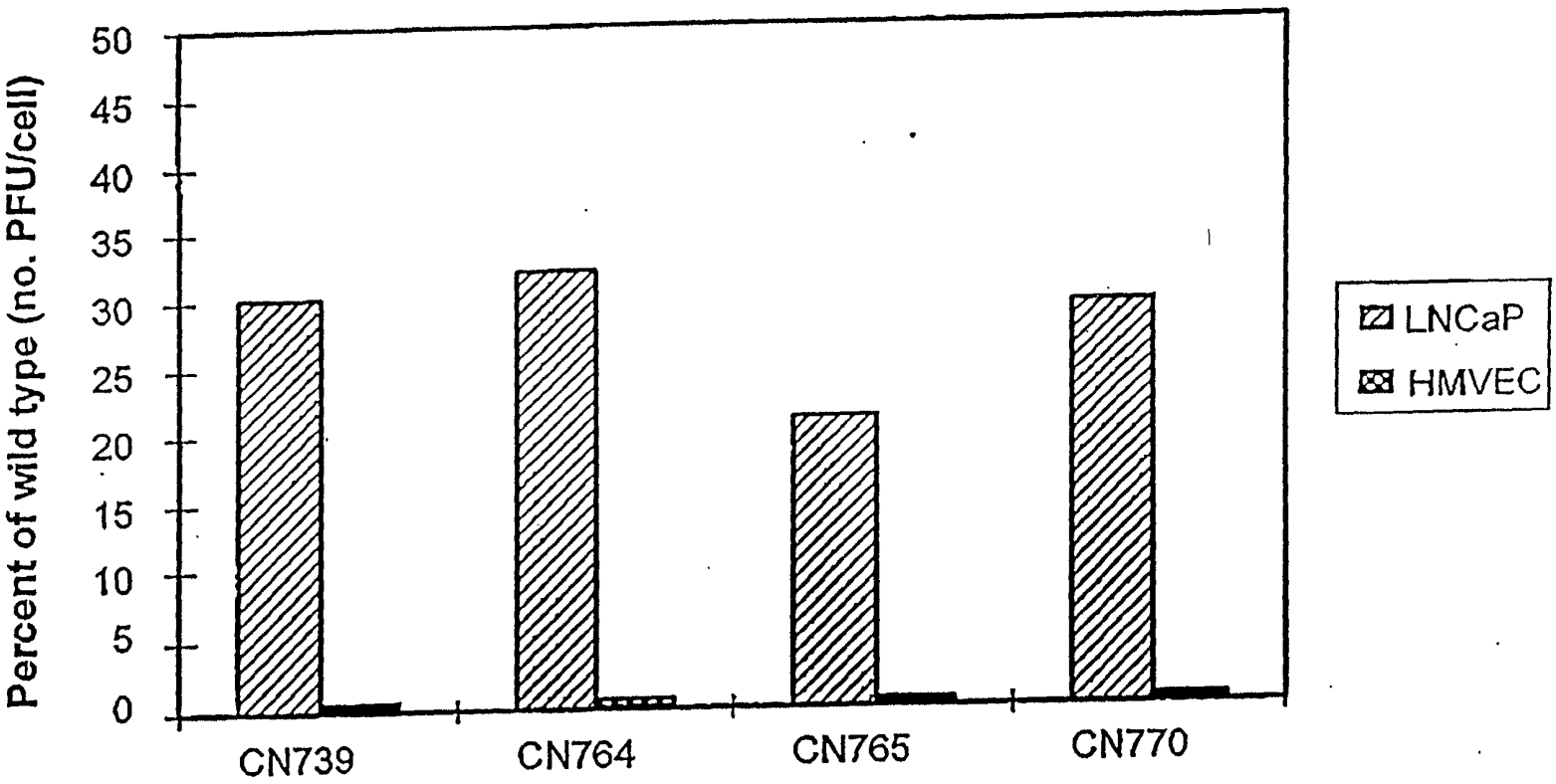


FIGURE 19

T05090 82257860

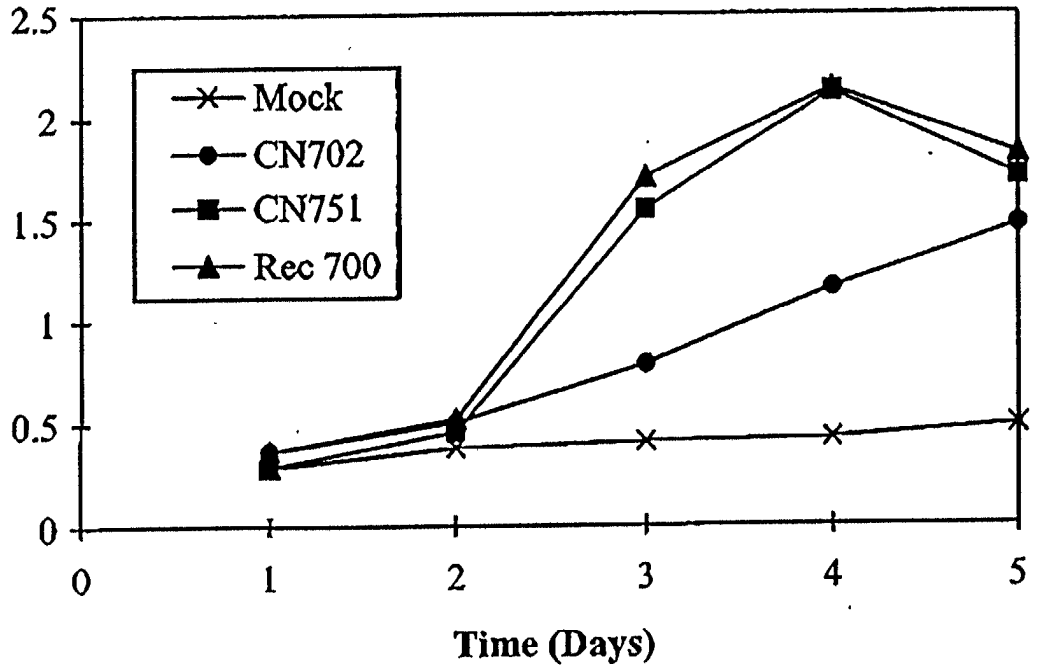


FIGURE 20

TDS090 B2B57860

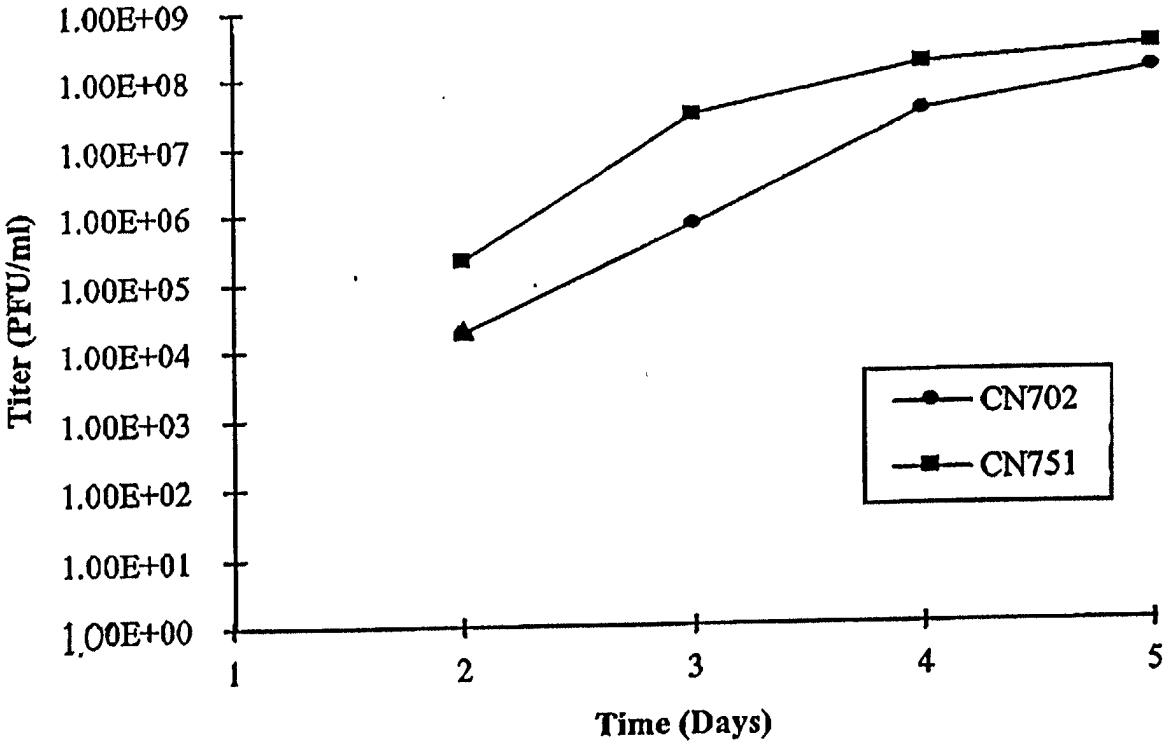


FIGURE 21

TO5090 "82215/2860

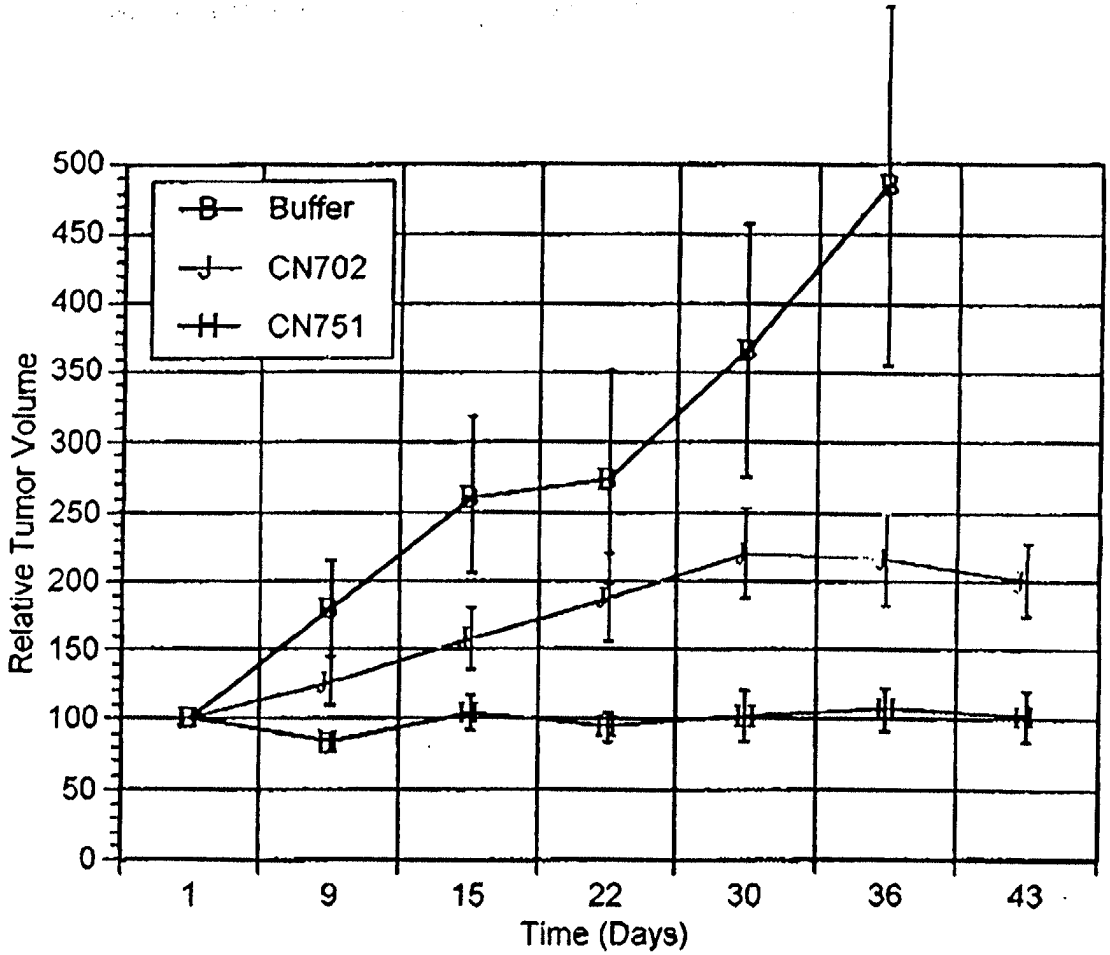


FIGURE 22

TOS090 82252860

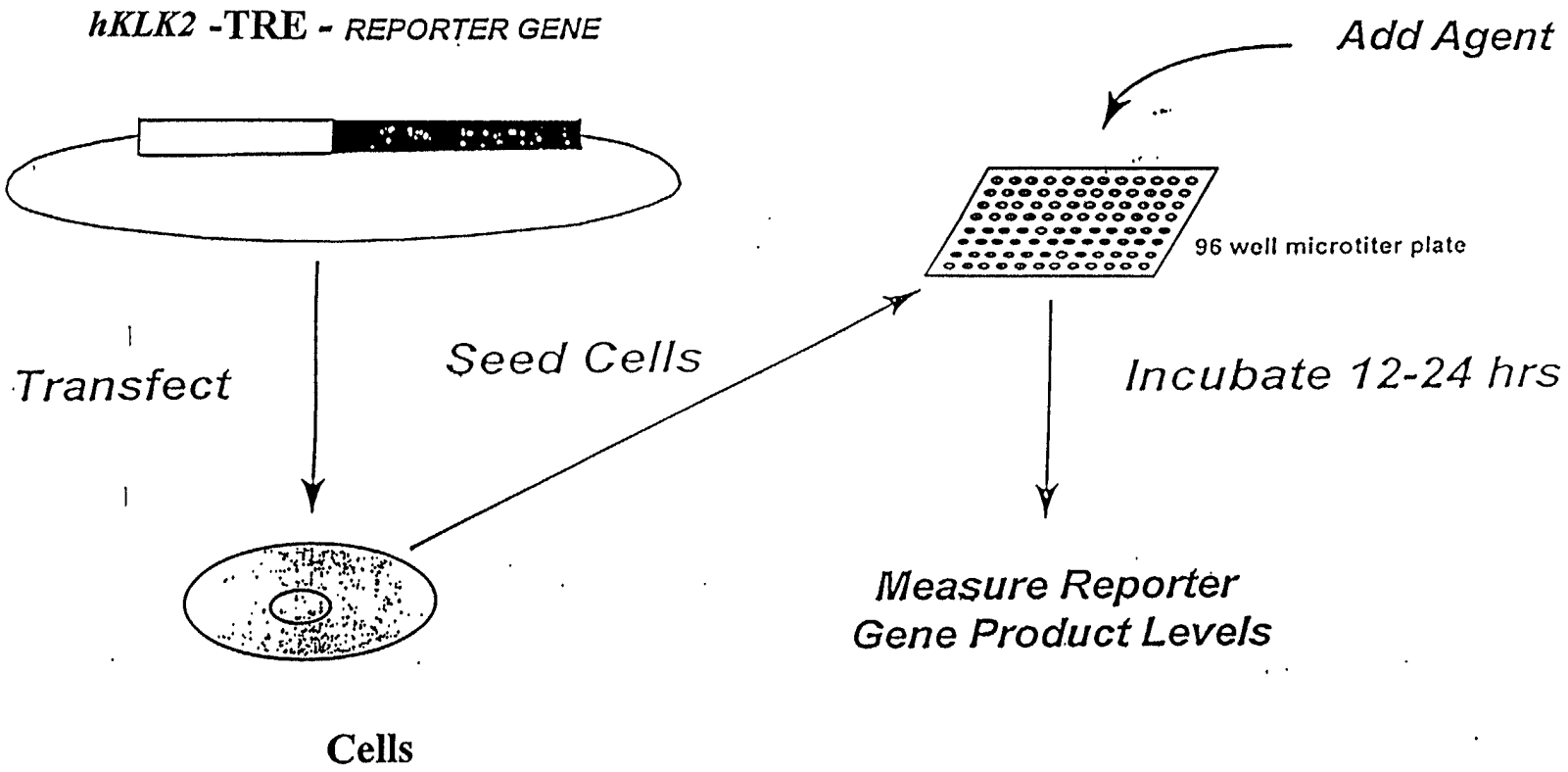


FIGURE 23A

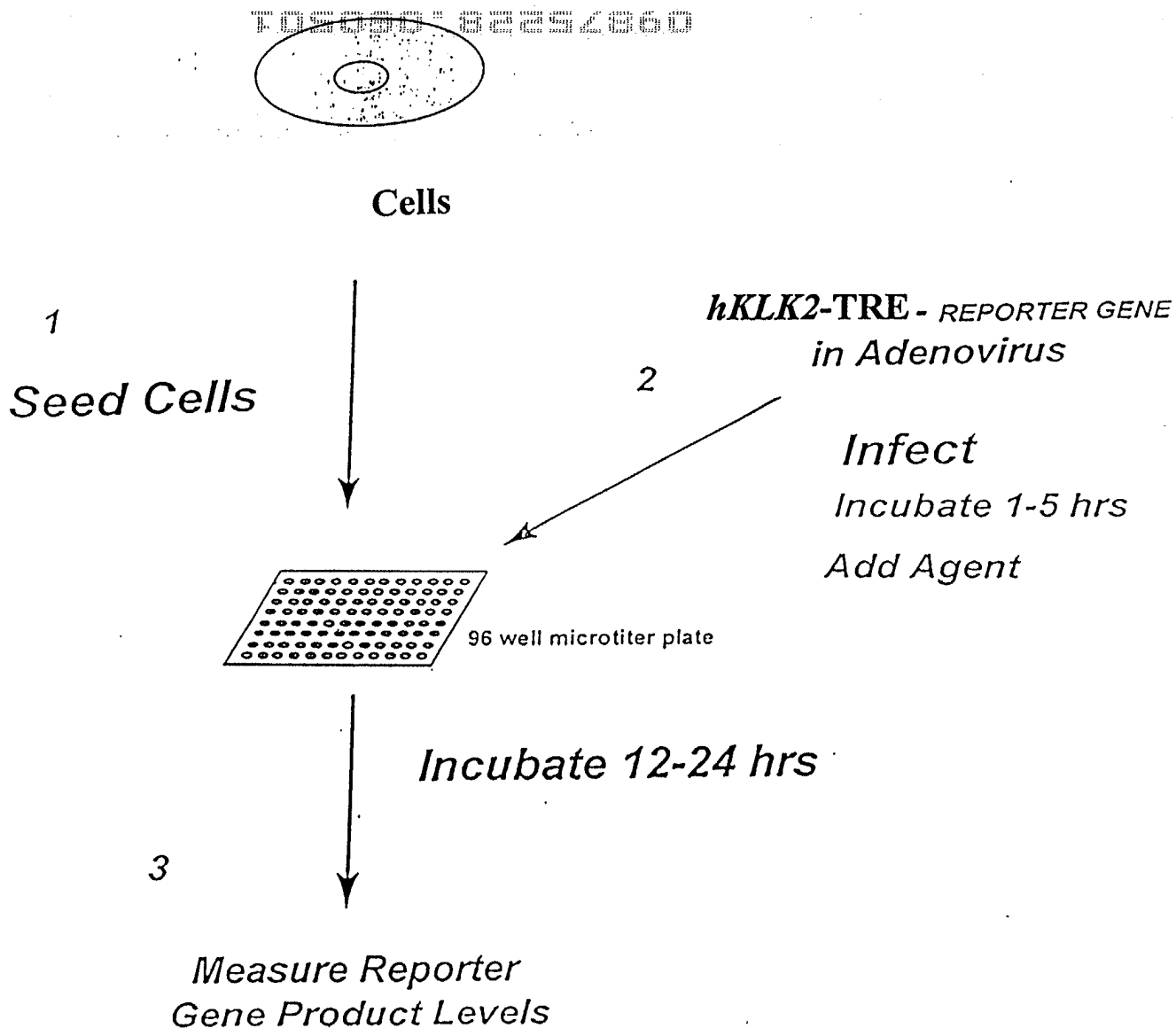

Cells
1
Seed Cells
2
hKLK2-TRE - REPORTER GENE
in Adenovirus
Infect
Incubate 1-5 hrs
Add Agent
96 well microtiter plate
Incubate 12-24 hrs
3
Measure Reporter
Gene Product Levels

FIGURE 23B

T05090 "82257860

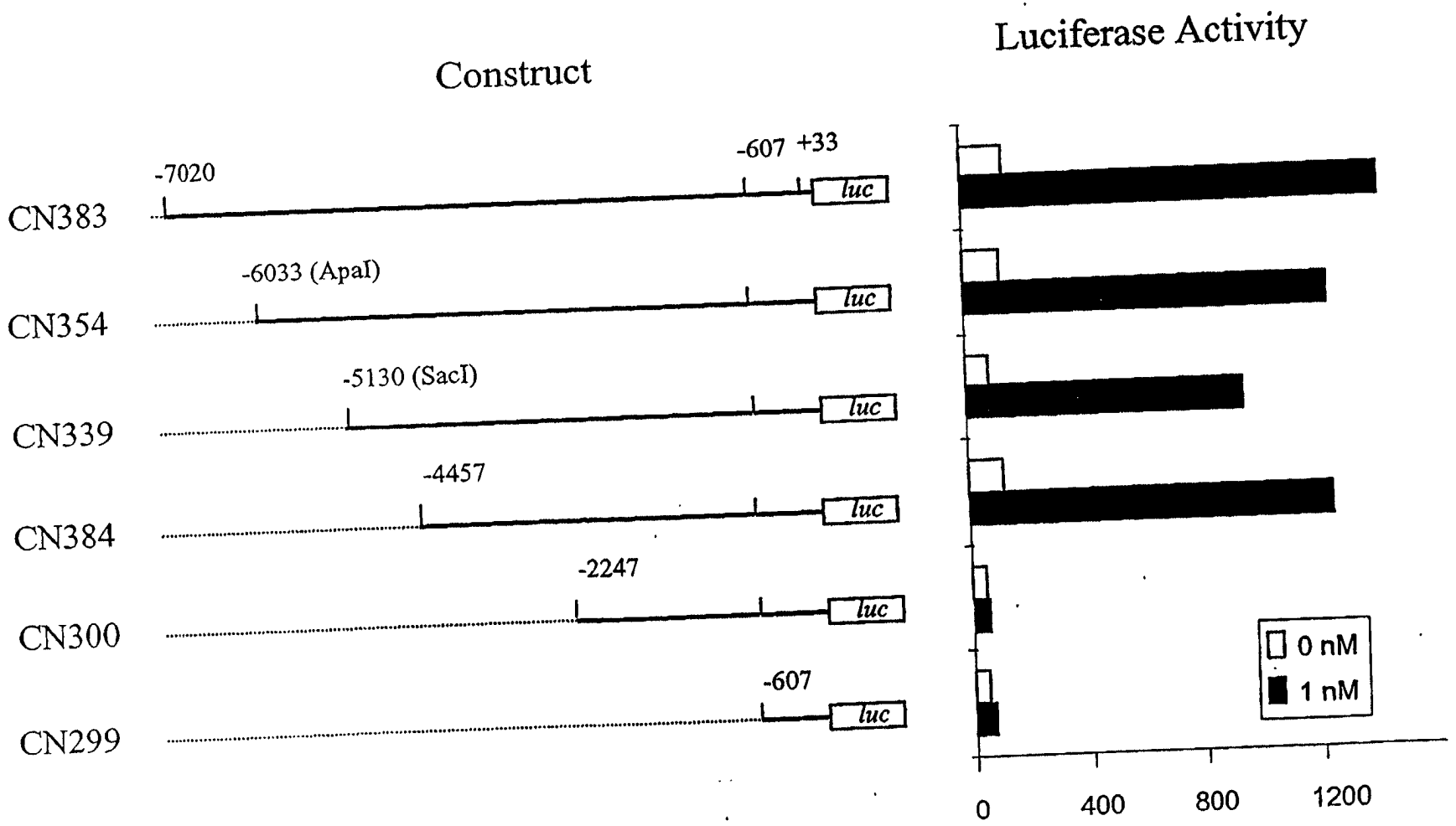


FIGURE 24A

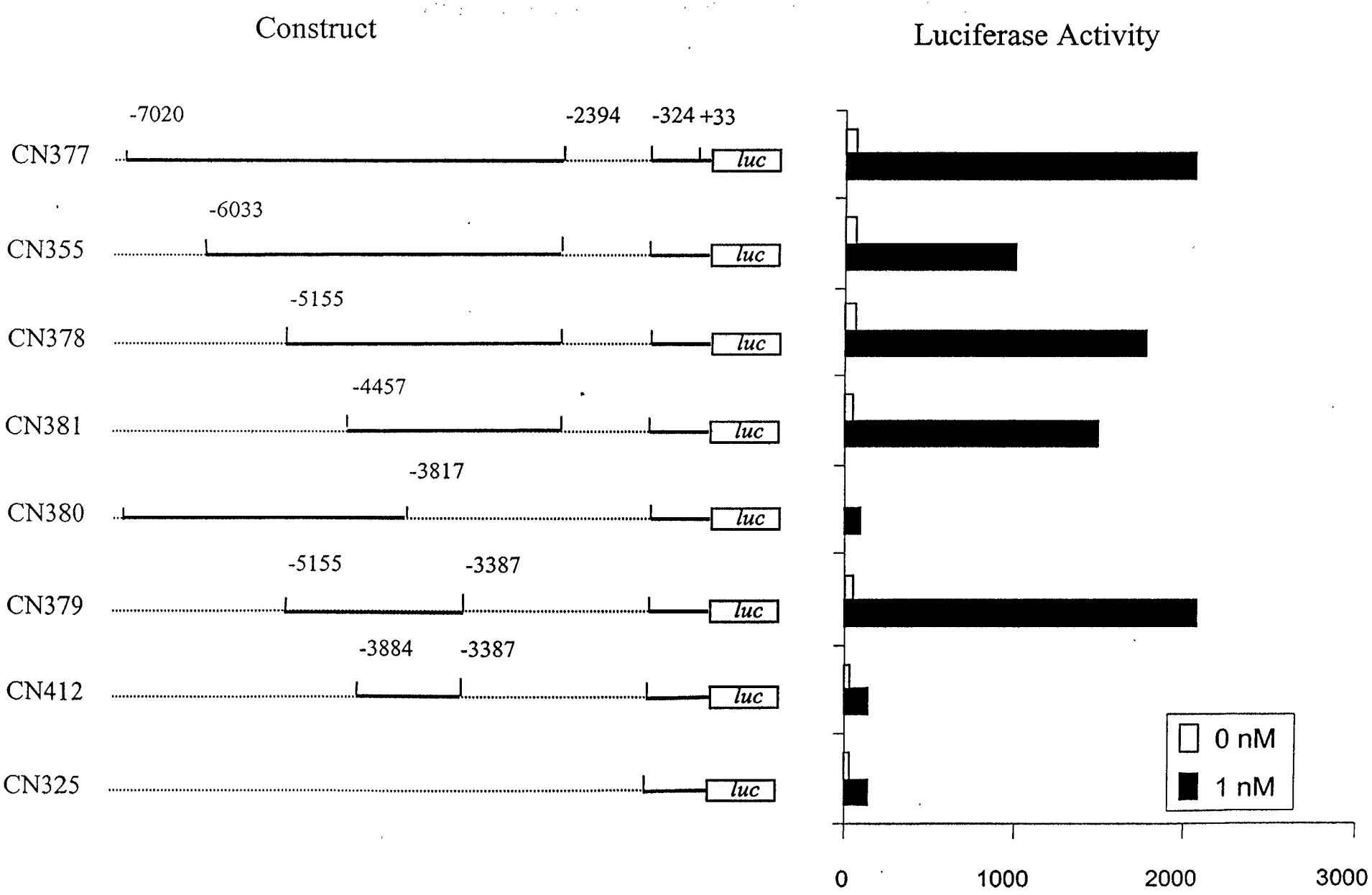

Construct
Luciferase Activity
-7020
-2394
-324
+33
CN377
luc
-6033
CN355
luc
-5155
CN378
luc
-4457
CN381
luc
-3817
CN380
luc
-5155
-3387
CN379
luc
-3884
-3387
CN412
luc
CN325
luc
0 nM
1 nM
0
1000
2000
3000

FIGURE 24B

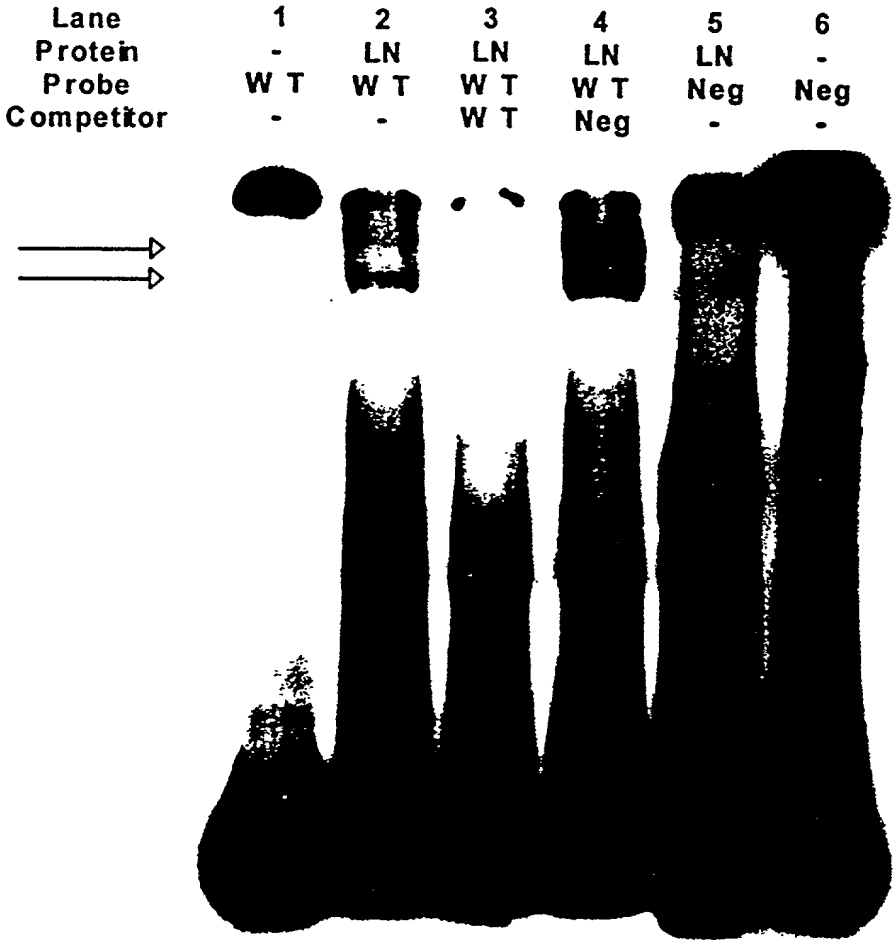

Lane 1 2 3 4 5 6
Protein - LN LN LN LN -
Probe WT WT WT WT Neg Neg
Competitor - - WT Neg - -

FIGURE 25A

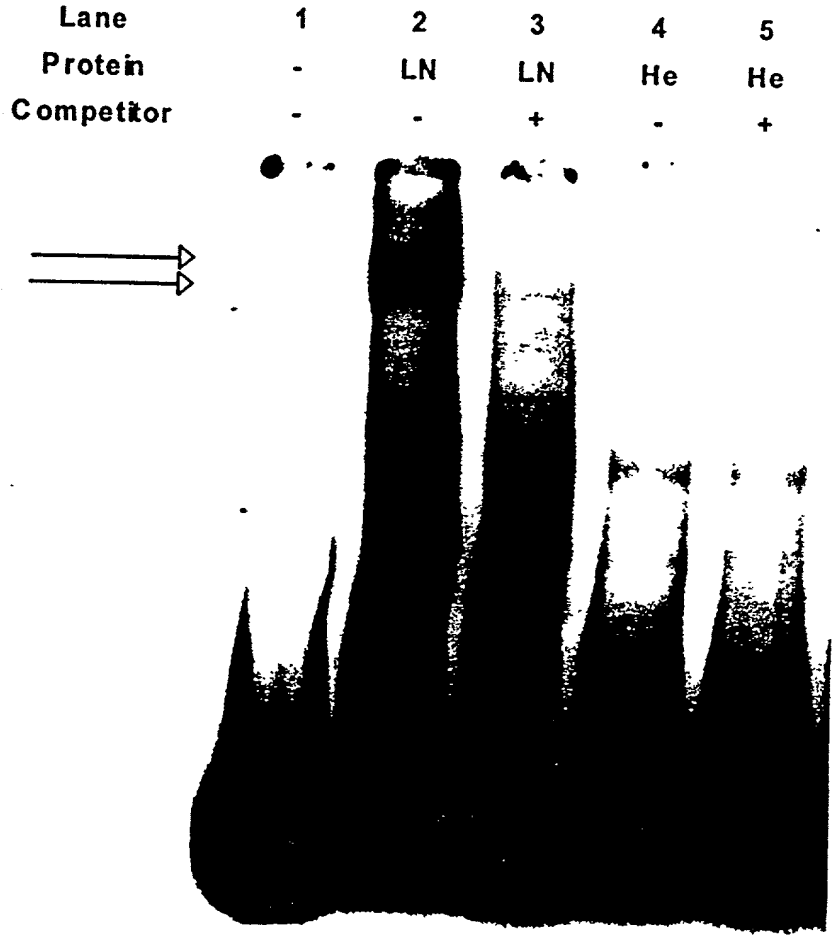


FIGURE 25B

T05090 82257360

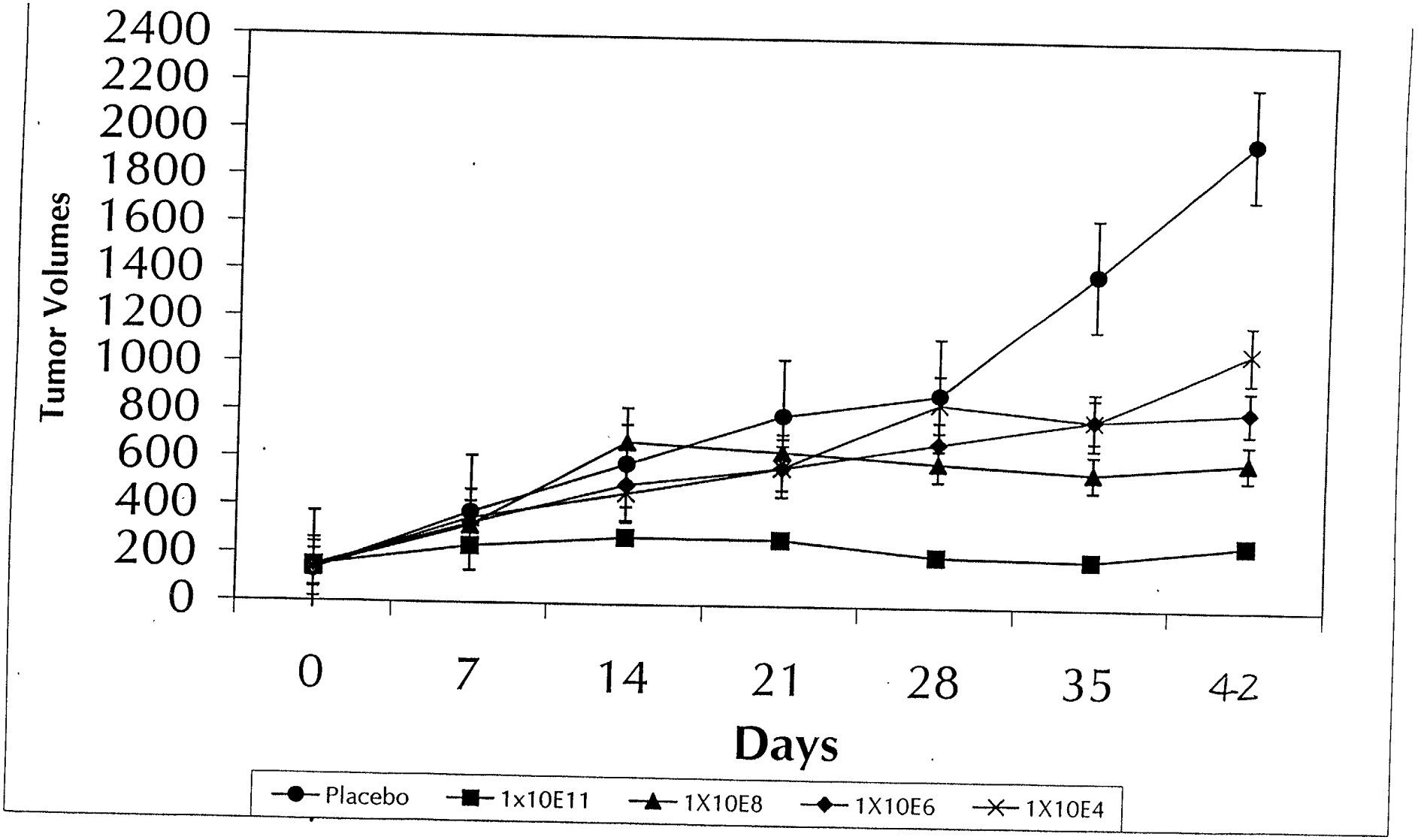


FIGURE 26